ALCOHOL WITHDRAWAL SYNDROME IN THE ELDERLY

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By

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ABSTRACT

INTRODUCTION: Alcohol withdrawal in older adults, despite being prevalent, is an understudied and thus poorly understood syndrome. The lack of evidence-based studies regarding presentation, diagnosis, treatment, and outcomes has led to poor recognition and often inadequate treatment of this syndrome in older adults.

MANUSCRIPT 1: Alcohol Withdrawal in the Elderly: A Systematic Review

OBJECTIVES: To identify the current evidence about alcohol withdrawal syndrome and treatment in older adults.

METHODS: Using the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement, we conducted a systematic review of articles from 1/1/1980-6/1/2012. The search included several databases and used plain language key words such as “alcohol withdrawal,” “alcohol withdrawal syndrome,” “alcohol withdrawal seizures,” “alcohol withdrawal delirium,” “ethanol withdrawal,” and “alcoholism.” Studies that included and/or focused on older adults were included. The details of the study design, participant characteristics, study setting, assessment, and outcome data were extracted from each of the included studies.

RESULTS: Seven studies were identified and all were descriptive cohort studies; 3 prospective, 2 retrospective, and 3 retrospective and prospective. All studies included both younger and older adults. More severe withdrawal was reported in several, but not all, studies. Similar findings were seen with

respect to duration of hospitalization, frequency of delirium tremens, and dosages of benzodiazepines.

CONCLUSIONS: The literature regarding older adults and alcohol withdrawal is limited with only seven studies to date. The small pool of existing literature provides no consensus on how older adults manifest with and are treated for alcohol withdrawal.

MANUSCRIPT II: Alcohol Withdrawal in the Elderly: A Descriptive Study

OBJECTIVES: To describe the population of older adults with alcohol withdrawal who present to the Emergency Department (ED) and are admitted to the hospital.

METHODS: We conducted a retrospective chart review of patients aged ≥ 65 years who presented to the ED and were admitted and treated for alcohol withdrawal syndrome (AWS). Potential patients were identified using ICD-9 codes for alcohol-induced mental disorders. Patients were excluded if no alcohol withdrawal treatment was administered or the subject was directly admitted to the psychiatry service. Data regarding demographics, symptoms, treatments, and outcomes were collected.

RESULTS: A total of 211 patients were screened and 90 (mean age 73 years, 59% men) were given a diagnosis of AWS and are included in this analysis. The most common physical comorbidity reported was hypertension (16%) and coronary artery disease (19%); 16% had multiple (≥ 3) major physical comorbidity. The chief complaint was alcohol-related (48%), trauma (30%), followed by psychiatric conditions (13%); 13% were suicidal at presentation. Tremors were documented in 42% of cases, and were present for 32%.

Hyperreflexia was not documented in 99% of cases. Tongue fasciculations were documented in 13% and were present in 10%. In total, 59% received at least one dose of a benzodiazepine in the ED; specifically lorazepam (12%), diazepam (21%) or chlordizepoxide (4%); an additional 22% received a combination of these. For 41%, no benzodiazepine was ordered in the ED. The standard Clinical Institute Withdrawal Assessment protocol was followed in 41%. Based on post-discharge surveillance, 36 patients (25%) presented to the ED again within 30 days; of these 18 had alcohol-related conditions, 10 had trauma, 3 had psychiatric conditions, and 14 had other diagnoses.

CONCLUSIONS: Commonly held notions that elderly patients with AWS are more likely to have multiple comorbidities, live alone, and present with a traumatic or infectious complaints, are not universally correct. ED physicians likely need to re-assess how they approach older adults, to raise their index of suspicion for alcohol withdrawal in this population, and to be more systematic and efficient in identifying older adults with AWS.

BIOGRAPHICAL SKETCH

Marianna Karounos earned a Bachelor of Arts in Psychology from New York University earning her Doctor of Osteopathic Medicine from the New York College of Osteopathic Medicine. She did her residency training in Emergency Medicine at St. Joseph's Regional Medical Center in Paterson New Jersey, followed by a fellowship in Geriatric Emergency Medicine at New York Presbyterian/Weill Cornell Medical College. She is currently an Assistant Professor of Clinical Emergency Medicine at New York Medical College and serves as Chief of the Geriatric Emergency Department at St. Joseph's Regional Medical Center in Paterson New Jersey. She is also a John A. Hartford Scholar and the current Chair of the Geriatric Emergency Medicine Section in the American College of Emergency Physicians. Her interests include substance abuse in the elderly and the role of palliative medicine in the Emergency Department. She aspires to continue to develop her career as an academic emergency physician and clinical researcher.

Dedicated to my husband Anastasios, and my three beautiful children

George, Christian, and Alexander

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Alcohol Withdrawal in the Elderly: A Systematic Review

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Alcohol Withdrawal in the Elderly: A Systematic Review

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CONFLICTS OF INTEREST NOTIFICATION PAGE

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ABSTRACT

OBJECTIVE: To identify the current existing evidence about alcohol withdrawal syndrome and treatment in older adults.

METHODS: Using the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement, we conducted a systematic review from 1/1/1980-6/1/2012. The search included several databases and used plain language key words such as “alcohol withdrawal,” “alcohol withdrawal syndrome,” “alcohol withdrawal seizures,” “alcohol withdrawal delirium,” “ethanol withdrawal,” and “alcoholism.” Studies that included and/or focused on older adults were included. The details of the study design, participant characteristics, study setting, assessment, and outcome data were extracted from each of the included studies.

RESULTS: Seven studies were identified and all were descriptive cohort studies; 3 prospective, 2 retrospective, and 3 retrospective and prospective. All the studies included subjects of all ages, young and old. A more severe withdrawal syndrome in older adults was identified in several studies, but other found no difference. The same finding was seen with respect to duration of hospitalization, frequency of delirium tremens, and dosage of benzodiazepines.

CONCLUSIONS: The literature regarding older adults and alcohol withdrawal is limited with only seven studies to date. Further, the small pool of existing literature provides no consensus on the details of how older adults manifest with and are treated for alcohol withdrawal.

INTRODUCTION

Excessive chronic alcohol consumption among older adults is a common but under-recognized public health issue.[1] Alcohol withdrawal syndrome (AWS), which may occur when a chronic user abruptly stops drinking alcohol, can have significant medical consequences.[2,3] If not recognized and aggressively treated early in the disease process, AWS may progress swiftly to seizures, delirium tremens, autonomic instability, and even death.[2,3] Most existing literature on AWS has focused on younger populations. AWS may have a more significant impact on older patients, who have less physiologic reserve, more medical co-morbidities, altered pharmacokinetics, increased CNS sensitivity to toxins, underlying cognitive deficits, longer duration of alcohol abuse, and greater susceptibility to medication-alcohol interactions.[1,4]

A better understanding of AWS in older adults is critical to improve its recognition and tailor its treatment in order to optimize care of these particularly vulnerable patients. Our research goal was to systematically identify existing evidence about alcohol withdrawal syndrome and treatment in older adults.

METHODS

The guidelines from the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement were followed.[5]

Protocol and Registration

Before conducting our review, we developed a comprehensive systematic review protocol in close consultation with a research librarian (DD). We registered our protocol with the International Prospective Register of Systematic Reviews (PROSPERO).[6] (It is available at: http://www.metaxis.com/prospero/full_doc.asp?RecordID=2581)

Search Strategy

We collaborated with a research librarian (DD) to develop a comprehensive search strategy. We searched MEDLINE, EMBASEM CINAHL, PsycINFO, Cochrane, Alcohol and Alcohol Problems Science Database, and Information on Drugs and Alcohol from 1/1/1980-6/1/2012. Our search employed the controlled vocabulary of each database and plain language and used: "alcohol withdrawal," "alcohol withdrawal syndrome," "alcohol withdrawal seizures," "alcohol withdrawal delirium," "ethanol withdrawal," and "alcoholism." We employed filters to effectively limit our search to identify geriatric patients.[7] The final search results were limited to human studies and English language studies using the limits provided within each database. We also evaluated reference lists of reviews and retrieved articles to check for additional studies. Our search strategy was independently evaluated by a research librarian who was not a member of the research team, with any suggestions incorporated.

Inclusion Criteria

Inclusion criteria were: original research studies analyzing presentation, natural history, complications and/or treatments of alcohol withdrawal syndrome that (1) used age as an analytic factor AND (2) included at least 10

subjects aged ≥ 55 OR at least 1 age category including only patients ≥ 55 OR with age range including patients ≥ 75.

Data Collection and Processing

Two study authors (MK, AK) independently and in duplicate screened and retrieved titles, abstracts, and full-text articles for inclusion using the pre-designed protocol. Those not meeting inclusion criteria were excluded based on the abstract, and full text of each potential article was obtained by each reviewer and evaluated. Data was collected and stored in EndNote software (Philadelphia, PA).[8] Disagreements about any study inclusions were resolved by consensus.

Data Extraction and Analysis

Details of the study design, participant characteristics, study setting, assessment, and outcome data were extracted from each of the included studies. Disagreements about extracted data were resolved by consensus. All studies were evaluated for potential confounding, measurement error, and selection bias. While the initial protocol had allowed for consideration of meta-analysis of results, this was abandoned given the small number of publications with varied methods that were obtained.

RESULTS

Search Results

The initial search identified 5,069 citations after duplicates were removed. After review of these titles and abstracts, 247 full text articles were retrieved

and reviewed in detail. Seven of these met inclusion criteria. The remaining were excluded for various reasons including not being focused on the syndrome of alcohol withdrawal, not using age as an analytic factor, or not containing at least 10 subjects $\geq$ 55 years of age in their study population. Details of our search results are shown in Figure 1.1.

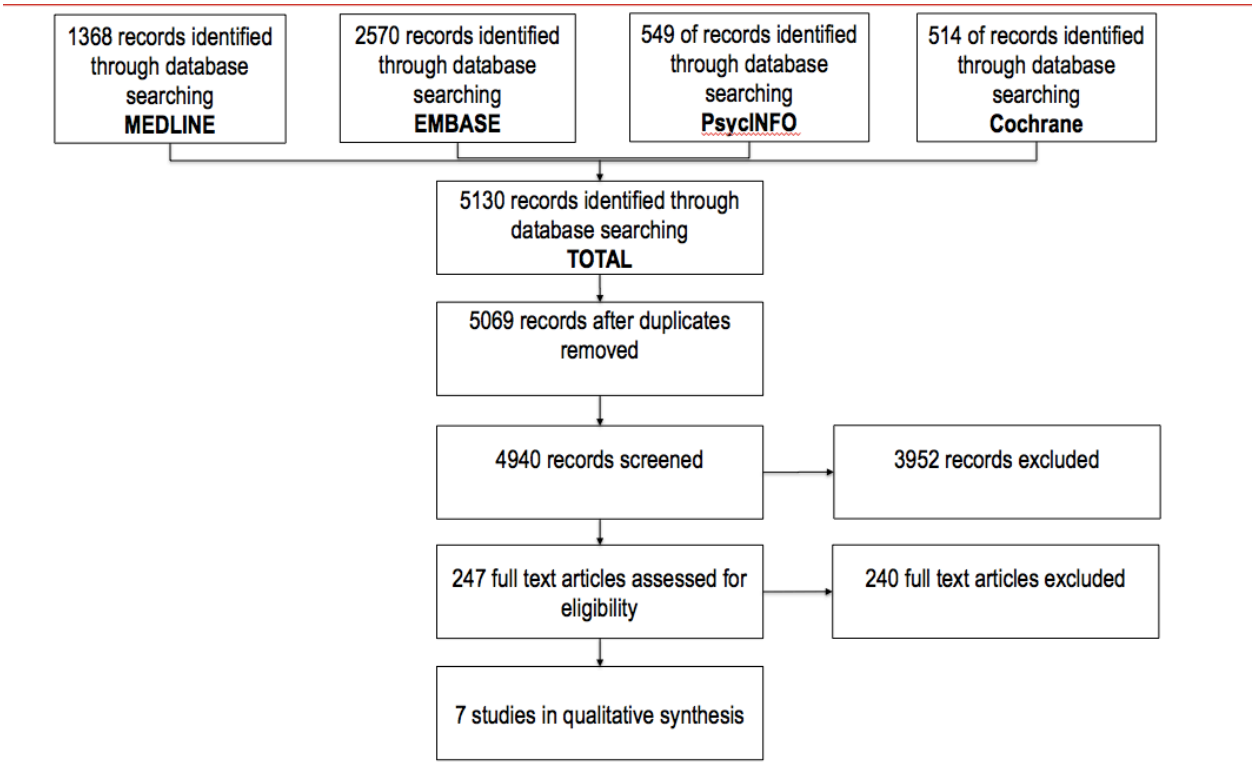

Figure 1.1: PRISMA Diagram

Description of Studies

A systematic review of 7 major electronic databases, including 3 that are solely focused on psychiatric, drug, and alcohol research, was conducted between the years 1/1/1980-6/1/2012 and revealed only 7 studies published between 1989 and 2001 that looked at alcohol withdrawal in the elderly population in some form. In addition to this low number of studies from which to draw conclusions, each study varied greatly with respect to the methodologies they employed. All were descriptive cohort studies; 3 prospective, 2 retrospective, and 3 retrospective and prospective. All the studies included subjects of all ages, young and old. None evaluated an intervention specifically directed at older withdrawal patients. Studies used different age categories for analysis, with some stratifying by decade and others variously defining older adults as ≥58, ≥60, or ≥70. Both the countries in which the studies were conducted, as well as the specific clinical settings for the studies were variable, therefore resulting in study populations that were highly heterogeneous. While the majority of the studies were conducted in the United States (4), the three studies with the largest numbers of subjects were conducted in Australia, Poland, and Germany, respectively.[9-11] The clinical setting of the studies revealed significant variation as well. Four were conducted at inpatient alcohol treatment facilities (community and academic centers), two in Internal Medicine inpatient service units (both academic centers), and one at an inpatient psychiatric unit of a psychiatric hospital. Interestingly, no studies were conducted in the Emergency Department, where the majority of alcohol withdrawal cases are likely to initially present. The age ranges for what was considered “geriatric” varied across many of the studies. Four studies used the same geriatric age definition of 60 years of age or

greater, however, the remaining 3 did not. For these remaining 3 studies, one used 58 years or greater, one used 70 years or greater, and one did not define an age cut off. Different scales were used to assess withdrawal symptoms. When evaluating alcohol withdrawal, several scales can be used. The Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA), is a 10-item scale used in the assessment and management of alcohol withdrawal. Each item is scored independently and then a sum is calculated. The maximum score is 67; mild alcohol withdrawal is a score of 15 or less, moderate 16-20, and severe greater than 20. The ten items evaluated are: nausea/vomiting, tremor, paroxysmal sweats, anxiety, agitation, tactile disturbances, auditory disturbances, visual disturbances, headache, orientation and clouded sensorium. The Alcohol Withdrawal Scale (AWS) is a modification of the CIWA. It is an 18-item scale and incorporates all of the items in the CIWA as well as items to measure level of benzodiazepine intoxication, which is seen frequently in patients being treated with benzodiazepines during the course of alcohol withdrawal. For our reviewed studies two used the CIWA scale, three used the AWS. The remaining studies used other assessment methods; one used criteria for the diagnosis of alcohol withdrawal as defined by the DSM III and one used no scale at all, opting instead to use a compilation of 17 withdrawal signs and symptoms to do their assessment. Characteristics of the 7 studies are described in detail in Table 1.1.

Table 1.1 Study Findings Summary

Study	Year & Country	Study Design & Setting	Ages & Sample Size	Measures & Assessments	Findings
Liskow et al.	1989 USA	Cohort Prospective Inpatient alcohol treatment units at Veterans Affairs Hospital	Older subjects aged 58-77 compared to younger subjects 26 older subjects in analysis compared to 24 younger subjects 103 total study subjects	- AWIS (Alcohol Withdrawal and Intoxication Scale - Dose of chlordiazepoxide given - duration of withdrawal	- Had higher AWIS scores (mean on day 1: 22.3 vs. 12.2 for younger subjects), suggesting an increased severity of withdrawal symptoms - had increased duration of withdrawal symptoms (mean AWIS score on day 5: 9.2 vs. 6.7 for younger subjects) - Required larger doses of chlordiazepoxide for symptom control (mean total dose day 1: 140.4mg vs 62.5mg for younger subjects, day 3: 85.5 mg vs. 20.8 mg)
Brower et al.	1994 USA	Cohort Retrospective 2 inpatient alcohol treatment programs (one specializing in treatment of older adults) at a community thospital	Older subjects aged ≥60 compared to: younger subjects aged 21-35 48 older subjects in analysis compared to: 36 younger subjects	chart review for: - documentation of 17 withdrawal symptoms - treatment regimen	- had increased number of withdrawal symptoms (mean total symptoms of 6.8 vs. 5.6 for younger subjects) - had increased duration of symptoms (mean last day of symptoms 9.0 vs. 6.5 for younger patients) - had no significant difference in required medication dose - had no significant difference in duration of medication treatment

Ferguson et al.	1996 USA	Cohort Retrospective Inpatient internal medicine service	Subjects aged: 19-78, mean 41.9 200 total study subjects	chart review for: - documentation of withdrawal symptoms consistent with DSM III diagnosis of delirium tremens	- DTs occurred with equal frequency among all age groups *- oldest subject experiencing DTs was 70 years old*
Foy et al.	1997 Australia	Cohort Prospective Inpatient internal medicine service	Older subjects aged ≥70 compared to: younger subjects aged <70 55 older subjects in analysis compared to: 484 younger subjects	-AWS (Alcohol Withdrawal Scale) (modification of the CIWA-A, previously published by the authors, 1986) -dose of diazepam given	Older adults: - had increased risk of complications (odds ratio=1.8) - had trend towards increased risk of delirium
Kraemer et al.	1997 USA	Cohort Retrospective and prospective Inpatient internal medicine service	Older subjects aged ≥60 compared to: younger subjects aged<60 84 older subjects in analysis compared to: 200 younger subjects	- CIWA-Ar (Revised Clinical Institute for Alcohol Withdrawal Scale) scores - dose of benzodiazepine given - duration of withdrawal - development of complications	Older adults (aged ≥60) - had increased risk of delirium (including but not limited to DTs) - had increased transient dependency in 2+ ADLs - had trend toward significant increase in witnessed falls - required more IV fluid administration - required use of restraints more frequently

Wetterling et al.	2001 Germany	cohort Prospective Inpatient alcohol treatment unit at an academic hospital	3 age groups used for analysis: <30, 30-59, ≥60 41 subjects aged ≥60 compared to: 611 subjects aged 30-59 compared to: 71 subjects aged <30	AWS (Alcohol Withdrawal Syndrome)	Older adults (aged ≥60): - had no significant difference in AWS scores - had no significant difference in duration of withdrawal (defined as AWS>3) - had more previous years of alcohol dependence - had trend towards more severe concomitant medical disorders - had trend towards less reported
Wojnar et al.	2001 Poland	Cohort Retrospective and prospective Inpatient general psychiatric hospital	5 age groups: <30, 30-39. 40-49, 50-59, ≥60 50 subjects aged ≥60 compared to:192 subjects aged 50-59 compared to:394 subjects aged 40-49 compared to:437 subjects aged 30-39 compared to: 140 subjects aged <30	-structured questionnaire completed by treating psychiatrists -CIWA-A scale (patients enrolled prospectively only, n=321)	Older adults (aged ≥60, comparing 5 age groups): - had no significant difference in severity of withdrawal symptoms - had no significant difference in incidence of DTs - had a greater frequency of hypertension, hypokalemia, other complications of alcohol withdrawal - had no significant difference in duration of withdrawal - had longer duration of hospitalization (mean length of stay 11.5 days for subjects aged ≥60 vs. 8.8 days in subjects aged ≤40) despite resolution of withdrawal - had no significant difference in required medication dose

Findings from Studies

Three studies found that adults ages ≥70, ≥58, and ≥60 respectively, had more severe withdrawal syndromes than younger patients as defined by one or more of the following: an increased number of withdrawal symptoms such as tachycardia, hypertension, tremor, and delirium, increased duration of symptoms, increased duration of hospitalization, higher doses of benzodiazepines required, higher CIWA or AWS scores overall.[9,12,13] Two studies found no difference in withdrawal severity among the age groups.[10,11]

Wojnar and Kraemer found that adults ≥60 years of age had a longer duration of hospitalization (11.5 days vs. 8.8 days and 5.9 days vs. 3.5 days respectively) for the treatment of their alcohol withdrawal[10,14] Two studies found that adults ≥58 years of age and ≥60 years of age, respectively, had a longer duration of alcohol withdrawal symptoms as shown by higher AWIS scores with one showing AWIS scores of >6 on day 5 as compared to the younger cohort whose AWIS scores were <7 on day 5, and the other showing symptoms persisting at day 9 of hospitalization while the younger cohort had symptom resolution before day 7. [12,13] But two others found no difference.[10,11]

Delirium tremens was found to be more common among older adults by Foy and Kraemer,[9,14] but two others found no difference.[10,15] Ferguson, Wetterling, and Wojnar all showed that regardless of the number of years of problem drinking or number of drinks in the most recent binge, adults ≥60 years of age developed clinically significant delirium, as defined by AWS and CIWA scores, at the same rates as their younger heavy drinking cohorts.[9-11] Furthermore, Foy and Kraemer showed that, in fact, adults ≥70 and ≥60 years

of age, respectively, were at higher risk than their younger cohorts at developing clinically significant delirium.[9,14]

The dosage of benzodiazepines needed for alcohol withdrawal treatment was also variable. Liskow observed that adults ≥58 years of age being treated for alcohol withdrawal required double and triple the amounts of Chlordiazepoxide (140.4mg vs. 62.5mg and 85.5mg vs. 20.8mg) for symptom control (tremors, sweating, nausea/vomiting, disorientation, hallucinations, delusions, agitation, tachycardia, seizures, ataxia, dysarthria, and nystagmus) on days 1 and 3, respectively.[12] However, two other studies found no difference in the dosage requirements between the age groups.[10,13]

Only Kraemer looked at restraint use and found that the use of restraints was more common in older adults (age ≥ 60) with alcohol withdrawal as compared to younger adults (age < 60) with rates of 11.9% versus 2.5%, respectively. However, the type of restraints and duration of their use was not described.[14] Four studies found that adults ≥58 or ≥60 years of age consumed less alcohol as compared to younger cohorts (204.1g/day vs. 288.3g/day, 172g/day vs. 214g/day, 207g/day vs. 219g/day, and 16 drinks/day vs. 20.5 drinks/day respectively) during the 30 days or the binge before presentation,[10-12,14] while one found no difference in alcohol consumption.[13]

DISCUSSION

Despite knowledge that alcohol abuse disorders and, in particular, alcohol withdrawal syndrome are increasing in prevalence in the elderly, very little research has been done to explore this growing health concern. As a result, a consensus regarding clinical approaches to diagnosis and treatment has not been reached. When considering these studies together, it is clear that alcohol

use and abuse, as well as the sequelae of alcohol withdrawal syndrome represent significant clinical problems in older adults. However, given the small number of studies and the great variability in the methodologies used by each study, we have a limited ability to extract many meaningful conclusions to help begin to close our knowledge gap.

Despite the numerous limitations of these studies, taken collectively, several preliminary insights about alcohol withdrawal in the elderly may be made that begin to better characterize this vulnerable population, the treatment they receive, and their hospital course. Two of the studies demonstrated that elderly patients being treated with benzodiazepines for alcohol withdrawal required equal cumulative doses and sometimes even higher and more frequent dosing as compared to their younger cohorts. [10,12-14] This is particularly interesting for several reasons. First, this is contrary to what we might expect --- given well-studied examples of the reduction in drug metabolism in the elderly --- namely, that this group of patients would require much lower doses in order to achieve the same effects.[16,17] However, this is not the case. Second, this finding goes against the current mantra in geriatric pharmacology of “start low and go slow”, and perhaps suggests that, in the setting of alcohol withdrawal, clinicians should consider treatment with the same doses of benzodiazepines as would be considered in younger patients.[18,19] A potential explanation is the possible existence and effect of kindling in this clinical setting. Perhaps elderly patients with repeated episodes of alcohol withdrawal suffer progressively more severe episodes of withdrawal symptoms and thus require the need for higher than expected subsequent doses of benzodiazepines.

While it may not be surprising that hospitalized elderly patients may be at higher risks for the complications associated with alcohol withdrawal such as seizures, elevated blood pressure, hypokalemia, and dehydration, as compared with younger adults given their multiple co-morbidities and age-related physiologic differences, it further emphasizes that elderly patients with alcohol withdrawal are at higher risk for hospital associated morbidity.

Another notable finding is that of rates of delirium. While research has already shown that older adults are more susceptible to delirium in a variety of clinical settings and that numerous causes and precipitants are contributing factors in the development of delirium, the toxicologic emergency of alcohol withdrawal may place the elderly at an even higher risk for both the development and the severity of delirium.[20-23] What can be concluded is that in older adults hospitalized with alcohol withdrawal syndrome, delirium is a serious complication.

Despite being mentioned in only the 1997 study done by Kraemer, the use of restraints warrants comment. Kraemer noted that restraint use was significantly higher in older adults with alcohol withdrawal as compared to younger adults. Because recent research has shown that restraint use in the elderly is not appropriate should be used rarely, if at all, this study's findings raise some questions.[24,25] Future research might look more closely at rates of restraint use in elderly patients with alcohol withdrawal and, in particular, the situations in which they are used and the outcomes of their use.

While kindling is a phenomenon associated mostly with benzodiazepine withdrawal, alcohol has a very similar mechanism of tolerance and withdrawal involving *gamma*-Aminobutyric acid (GABA) and N-methyl-D-aspartate (NMDA) receptors.[26,27] Upon review of these studies, there may be occurring

some type of ‘kindling effect’ in elderly patients with chronic alcohol use or abuse that may partially be explained by their age-related changes in both pharmacokinetics and pharmacodynamics. Wojnar, Liskow, and Wetterling all demonstrated that elderly patients suffering from clinically significant alcohol withdrawal had in fact consumed less alcohol in the recent days surrounding the commencement of their withdrawal episode compared to younger cohorts, suggesting that their withdrawal occurred after deviating from lower baseline alcohol levels.[10-12] This may be explained by kindling if the hypothesis holds true that this age group has had more years of alcohol abuse and subsequent episodes of detoxifications.

Although some notable conclusions can be drawn from the limited amount of available research, it is clear that there are still many unanswered questions. Alcohol withdrawal in the elderly population remains a significantly under-recognized clinical entity and a grossly understudied phenomenon. While much more research needs to be done, some of the limitations concluded as a result of this systematic review must be addressed. Standardizing methodologies would be of critical importance. Adopting the currently accepted age definition for geriatrics of $\geq$65, employing standardized scales such as CIWA, since it has been validated in a number of settings both impatient and outpatient, and selecting similar outcomes to measure, such as length of stay, rates of delirium, frequency of electrolyte disturbances, dosing of benzodiazepines, and frequency of vital sign abnormalities, and would prove to be important so that groups could be more easily compared and analyzed so that subsequent conclusions may be made more accurately.

Several future key topics warrant exploration and expansion. One important subject is the potential delay in the diagnosis of alcohol withdrawal.

A core concept in geriatric emergency medicine is that of atypical disease presentation. In older adults, common disease entities very frequently present atypically, such as altered mentation in sepsis, abdominal discomfort in acute myocardial infarction, and absence of cough in pneumonia to name a few.[28] It seems plausible that the potential for atypical disease presentation in the elderly, coupled with aging physiology, poorer baseline cognitive function, and potential under-estimation or frank ignorance on the part of the clinician regarding alcohol consumption in the elderly, makes a delay in diagnosis very likely. If, in fact, delays in diagnosis do exist, what impact does this have on the management and outcomes of this patient population? This is yet another topic that might be helpful to focus on in this patient population when they present to the Emergency Department (ED). The ED is where the majority of these patients get admitted for alcohol withdrawal, and they do not always present clearly to the ED physician. Perhaps looking at the barriers in identifying these patients in the ED would be of importance in beginning to understand their atypical presentations and allowing us to better manage them from the initial stages of alcohol withdrawal. This may have the potential ultimately to decrease morbidity and mortality in this growing and vulnerable population.

References

1. Caputo F, Vignoli T, Leggio L, Addolorato G, Zoli G, Bernardi M. Alcohol use disorders in the elderly: a brief overview from epidemiology to treatment options. Experimental gerontology 2012;47:411-6.

2. Sarff M, Gold JA. Alcohol withdrawal syndromes in the intensive care unit. Critical care medicine 2010;38:S494-501.

3. Stehman CR, Mycyk MB. A rational approach to the treatment of alcohol withdrawal in the ED. The American journal of emergency medicine 2013;31:734-42.

4. Scott RB, Mitchell MC. Aging, alcohol, and the liver. Journal of the American Geriatrics Society 1988;36:255-65.

5. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Journal of clinical epidemiology 2009;62:e1-34.

6. Booth A, Clarke M, Dooley G, et al. The nuts and bolts of PROSPERO: an international prospective register of systematic reviews. Systematic reviews 2012;1:2.

7. van de Glind EM, van Munster BC, Spijker R, Scholten RJ, Hooft L. Search filters to identify geriatric medicine in Medline. Journal of the American Medical Informatics Association : JAMIA 2012;19:468-72.

8. King R, Hooper B, Wood W. Using bibliographic software to appraise and code data in educational systematic review research. Medical teacher 2011;33:719-23.

9. Foy A, Kay J, Taylor A. The course of alcohol withdrawal in a general hospital. QJM : monthly journal of the Association of Physicians 1997;90:253-61.

10. Wojnar M, Wasilewski D, Zmigrodzka I, Grobel I. Age-related differences in the course of alcohol withdrawal in hospitalized patients. Alcohol and alcoholism 2001;36:577-83.

11. Wetterling T, Driessen M, Kanitz RD, Junghanns K. The severity of alcohol withdrawal is not age dependent. Alcohol and alcoholism 2001;36:75-8.

12. Liskow BI, Rinck C, Campbell J, DeSouza C. Alcohol withdrawal in the elderly. Journal of studies on alcohol 1989;50:414-21.

13. Brower KJ, Mudd S, Blow FC, Young JP, Hill EM. Severity and treatment of alcohol withdrawal in elderly versus younger patients. Alcoholism, clinical and experimental research 1994;18:196-201.

14. Kraemer KL, Mayo-Smith MF, Calkins DR. Impact of age on the severity, course, and complications of alcohol withdrawal. Archives of internal medicine 1997;157:2234-41.

15. Ferguson JA, Suelzer CJ, Eckert GJ, Zhou XH, Dittus RS. Risk factors for delirium tremens development. Journal of general internal medicine 1996;11:410-4.

16. Kitani K. Hepatic drug metabolism in the elderly. Hepatology 1986;6:316-9.

17. Kinirons MT, O'Mahony MS. Drug metabolism and ageing. British journal of clinical pharmacology 2004;57:540-4.

18. Moore AR, O'Keeffe ST. Drug-induced cognitive impairment in the elderly. Drugs & aging 1999;15:15-28.

19. Pasero CL, McCaffery M. Managing postoperative pain in the elderly. The American journal of nursing 1996;96:38-45; quiz 6.

20. Alagiakrishnan K, Wiens CA. An approach to drug induced delirium in the elderly. Postgraduate medical journal 2004;80:388-93.

21. Inouye SK. Delirium in hospitalized older patients. Clinics in geriatric medicine 1998;14:745-64.

22. Jacobson SA. Delirium in the elderly. The Psychiatric clinics of North America 1997;20:91-110.

23. Leentjens AF, van der Mast RC. Delirium in elderly people: an update. Current opinion in psychiatry 2005;18:325-30.

24. Hamers JP, Huizing AR. Why do we use physical restraints in the elderly? Zeitschrift fur Gerontologie und Geriatrie 2005;38:19-25.

25. Frank C, Hodgetts G, Puxty J. Safety and efficacy of physical restraints for the elderly. Review of the evidence. Canadian family physician Medecin de famille canadien 1996;42:2402-9.

26. Maldonado JR, Sher Y, Ashouri JF, et al. The "Prediction of Alcohol Withdrawal Severity Scale" (PAWSS): systematic literature review and pilot study of a new scale for the prediction of complicated alcohol withdrawal syndrome. Alcohol 2014;48:375-90.

27. Becker HC. The alcohol withdrawal "kindling" phenomenon: clinical and experimental findings. Alcoholism, clinical and experimental research 1996;20:121A-4A.

28. Jarrett PG, Rockwood K, Carver D, Stolee P, Cosway S. Illness presentation in elderly patients. Archives of internal medicine 1995;155:1060-4.

CHAPTER 2:

Alcohol Withdrawal in the Elderly: A Descriptive Study

TITLE PAGE

Alcohol Withdrawal in the Elderly: A Descriptive Study

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There are no conflicts of interest to report.

ABSTRACT

OBJECTIVE: To describe the population of older adults with alcohol withdrawal who present to the Emergency Department (ED) and are admitted to the hospital.

DESIGN: Retrospective chart review

METHODS: We conducted a retrospective chart review of patients aged ≥ 65 years who presented to the ED and were admitted and treated for alcohol withdrawal syndrome (AWS). Potential patients were identified using ICD-9 diagnosis codes for alcohol-induced mental disorders (291.0-291.89). Patients were excluded if no alcohol withdrawal treatment was administered or the subject was directly admitted to the psychiatry service. Data regarding demographics, symptoms, treatments, and outcomes were. Results were presented as proportions, means and standard deviations, and medians with interquartile ranges.

RESULTS: A total of 211 patients were screened and 90 were given a diagnosis of AWS and are included in this analysis. The mean age of the sample was 73 years and 59% were men. The most common physical comorbidity reported was hypertension (16%) and coronary artery disease (19%); 16% had multiple (≥ 3) major medical comorbidity. The chief complaint

was alcohol-related (48%), trauma (30%), followed by psychiatric conditions (13%); 13% were suicidal at presentation. Tremors were documented in 42% of cases, and were present for 32% and not present for 10%. Hyperreflexia was not documented in 99% of cases. Tongue fasciculations were documented in 13% and were present in 10% and not present in 3%. In total, 59% received at least one dose of a benzodiazepine in the ED; specifically lorazepam (12%), diazepam (21%) or chlordizepoxide (4%); an additional 22% received a combination of these. For 41%, no benzodiazepine was ordered in the ED. The standard Clinical Institute Withdrawal Assessment protocol was followed in 41%. The discharge destination was to home for 56%, to a monitored setting for 29%, and to a detoxification facility for 6%. Based on post-discharge surveillance, 36 patients (25%) presented to the ED again within 30 days; of these 18 had alcohol-related conditions, 10 had trauma, 3 had psychiatric conditions, and 14 had other diagnoses.

CONCLUSION: Our study demonstrates that commonly held notions that elderly patients with AWS are more likely to have multiple comorbidities, live alone, and present with a traumatic or infectious complaints, is not universally correct. Going forward, ED physicians likely need to reassess how they approach older adults, to raise their index of suspicion for alcohol withdrawal in this population, and to be more systematic and efficient in identifying older adults with AWS.

INTRODUCTION

Excessive chronic alcohol consumption among older adults is a common but under-recognized entity. Alcohol withdrawal syndrome (AWS), which can occur when a chronic user abruptly stops alcohol intake, can be associated with severe and sometimes life threatening complications. If AWS goes unrecognized and does not receive aggressive treatment early in its course, such as when a patient presents in the Emergency Department (ED), it can quickly progress to complications such as seizures, delirium tremens, autonomic instability, and even death.[9]

Currently there is little information about AWS in older adults; most information pertains to younger patients. While features of AWS in younger patients potentially could be extrapolated to older patients, aspects of the syndrome may be unique to older adults. For example, there may be physiologic differences between the age groups that influence presentation and subsequent clinical course.[28] These may include well-known aspects of health in older adults, such as less physiologic reserve, more medical comorbidity, altered pharmacokinetics, increased central nervous system sensitivity to toxins, underlying cognitive deficits, and greater susceptibility to medication-alcohol interactions.[17,28]

A better understanding of AWS in older adults is critical to improve its early recognition in the ED and tailor its treatment in order to optimize care for these particularly vulnerable patients. The goal of this study was to describe a sample of older adults admitted with alcohol withdrawal at our academic medical center in an attempt to better characterize these patients as they presented to the ED.

METHODS

We conducted a retrospective chart review of patients aged ≥ 65 years who presented to the ED and were admitted and treated for alcohol withdrawal at a large, urban, academic medical center from 1/1/08 – 3/31/12. Potential patients were identified using ICD-9 diagnosis codes for alcohol-induced mental disorders (291.0-291.89). Patients were excluded if no alcohol withdrawal treatment was administered or the subject was directly admitted to the psychiatry service.

We comprehensively reviewed the ED and hospital charts of each patient and each admission (including multiple admissions for patients with repeated visits) to collect information about demographics, vital signs, medication orders, laboratory test results, and treatments received in the ED and hospital as documented by ED staff and in-patient physicians, nurses, psychiatrists, physical therapists, and social workers. Data were abstracted from the medical records systematically using a standardized data abstraction protocol we developed before beginning chart review. This protocol included hierarchies of data sources for each data point to resolve any internal inconsistencies within the medical record. For example, for marital status, the social worker's documentation was considered most accurate. If the social worker's documentation was not available or did not include this information, we would record, in order, information from a psychiatry consultant, the admitting physician, and administrative records. Developing this protocol was critical because we encountered frequent internal inconsistencies within the medical record. This situation was anticipated as it is commonly encountered

when conducting research with chronic substance users who may not divulge information or be truthful with health care personnel.

Data were entered into a customized, secure, online, HIPPA compliant, REDCap database. Data analysis was conducted using STATA v12.0 (Stata Corp, College Station, TX). Results are presented as proportions, means and standard deviations, and medians with interquartile ranges.

This study was approved by the Weill Cornell Medical College Institutional Review Board.

RESULTS

To total, 211 patients were screened and 90 were given a diagnosis of AWS and are included in this analysis. The mean age of the sample was 73 years and 59% were men (Table 2.1). Approximately one quarter were currently married and most (61%) lived alone; 7% were undomiciled. Most patients did not report illicit drug use and most reported being current (32%) or former (30%) smokers.

The most common physical comorbidity reported was hypertension (16%) and coronary artery disease (19%); 16% had multiple (≥ 3) major medical comorbidity (Table 2.2). The prevalence of mental health comorbidity, however, was higher (35%), with the most common conditions being depression (23%) and anxiety (10%). Approximately one quarter reported taking prescribed out-patient opioids or benzodiazepines. The vast majority of patients (91%) reported a history of alcohol use/abuse and 15% reported

previous treatment in a detoxification facility. Approximately one quarter reported being treated for alcohol withdrawal in the past; symptoms included seizures (16%) and delirium tremens (10%).

These 90 patients had a total of 145 visits to the ED for AWS during the study period (18 patients had multiple visits, specifically 72 had 1 visit, 16 had 2 visits, 2 had ≥ 3 visits). For the majority of visits patients presented to the ED by ambulance (74%) and were not accompanied by family or an aide (63%) (Table 2.3). The chief complaint was alcohol-related (48%), trauma (30%), followed by psychiatric conditions (13%); 13% were suicidal at presentation. With respect to vital signs potentially associated with withdrawal, at triage 40% of cases had a heart rate ≥ 100 beats per minute and 32% had a systolic blood pressure ≥ 160 mmHg or a diastolic blood pressure ≥ 100 mmHg; 14% had both tachycardia and elevated blood pressure. 31% of cases were considered intoxicated on arrival; however, this information was not documented for 34%.

ED physical examination records were reviewed for specific features associated with withdrawal, such as tremors, hyperreflexia, and tongue fasiculations. Tremors were documented in 42% of cases, and were present for 32% and not present for 10% (Table 2.4). Hyperreflexia was not documented in 99% of cases. Tongue fasciculations were documented in 13% and were present in 10% and not present in in 3%. A blood alcohol level was ordered for 61%. In total, 59% received at least one dose of a benzodiazepine in the ED; specifically Lorazepam (12%), Diazepam (21%) or Chlordizepoxide (4%); an additional 22% received a combination of these. For 41%, no benzodiazepine was ordered in the ED.

All patients were admitted to the hospital, either to a regular floor (66%), a step-down unit (19%), or an intensive care unit (6%); 3% were admitted and discharged from the ED before receiving an inpatient bed assignment (Table 2.5). A total of 93% received benzodiazepines and standard Clinical Institute Withdrawal Assessment (CIWA) protocol was followed in 41%. The CIWA is a 10-item scale that assesses nausea/vomiting, tremor, paroxysmal sweats, anxiety, agitation, headache, orientation, clouded sensorium, and tactile, auditory, and visual disturbances. A social worker and psychiatric consultation was obtained for 52% and 23%, respectively. The median length of stay was 6 days; and in several cases (9) left against medical advice after a median of 2 days.

Two patients died during the hospitalization (respiratory failure and ventricular fibrillation cardiac arrest). The discharge destination was to home for 56%, to a monitored setting (i.e. nursing home, acute/subacute facility) for 29%, and to a detoxification facility for 6%. Most patients were referred for additional medical care, including Alcoholics Anonymous (75%), but fewer were referred for psychiatric follow-up (17%). Based on post-discharge surveillance of ED records, 36 patients (25%) presented to the ED again within 30 days; of these 18 had alcohol-related conditions, 10 had trauma, 3 had psychiatric conditions, and 14 had other diagnoses.

Table 2.1: Demographics, Social Characteristics & Reported Illicit Substance Use among Patients Age ≥65 Admitted from the Emergency Department for Treatment of Alcohol Withdrawal, Jan 2008-Mar 2012

	N = 90 patients
Age, years (mean ± SD)	73 ± 6 Range: 65 – 89
Male	53 (59%)
Marital Status	
Single	49 (54%)
Married	23 (26%)
Divorced	7 (8%)
Widowed	11 (12%)
Living Situation	
Alone	55 (61%)
With spouse	19 (21%)
With Family	5 (6%)
With Friend(s)	2 (2%)
Nursing Home	1 (1%)
Undomiciled	6 (7%)
Other	2 (2%)
Not Documented	--
Smoking Status	
Never	23 (26%)

Former	27 (30%)
Current	29 (32%)
Not Documented	11 (12%)
Illicit Drug Use	
Past	8 (9%)
Current (n=8)	2 (25%)

Results presented as n (%) unless otherwise specified. For individuals with more than one visit during the study period, results are presented for the first visit during the study period.

SD denotes standard deviation.

Table 2.2: Medical, Psychiatric & Alcohol Use History among Patients Age ≥65 Admitted from the Emergency Department for Treatment of Alcohol Withdrawal, Jan 2008-Mar 2012

	N = 90 patients
Medical Comorbidities (n=88)	
Cardiovascular	
Hypertension	51 (58%)
Coronary Artery Disease	17 (19%)
Atrial Fibrillation	5 (6%)
Liver	
Hepatitis B/C	3 (3%)
Cirrhosis	2 (2%)
Gastrointestinal	
Chronic Pancreatitis	2 (2%)
Peptic Ulcer Disease	5 (6%)
Neurologic	
Dementia	5 (6%)
Seizure	1 (1%)
CVA	3 (3%)
Anemia	1 (1%)
COPD/ Asthma	8 (10%)
Diabetes	11 (13%)
3+ comorbidities	14 (16%)

Any PMH psychiatric conditions (n=89)	31 (35%)
Depression	21 (23%)
Anxiety	9 (10%)
Bipolar	4 (4%)
PTSD	1 (1%)
Schizophrenia	0 (0%)
Other Behavioral Health	6 (7%)
Medications Taken at Home	
Opioids (n=86)	6 (7%)
Benzodiazepine (n=85)	14 (16%)
Alcohol History	
Alcohol use/abuse listed in medical record	81 (91%)
Weekly quantity of alcohol normally consumed, (number of drinks) median (IQR)	42 (21 – 79)
Previous treatment in detox facility	13 (15%)

Table 2.2: (continued)

Withdrawal History	
Alcohol withdrawal listed in medical record	20 (23%)
Treated for alcohol withdrawal in past	23 (26%)
Previous seizures with alcohol withdrawal	14 (16%)
Hallucinations with alcohol withdrawal	2 (1%)
Previous ICU for alcohol withdrawal	1 (1%)
Previous Delirium Tremens	9 (10%)
Admitted multiple times for withdrawal during study period	18 (20%)

Results presented as n (%) unless otherwise specified. For individuals with more than one visit during the study period, results are presented for the first visit during the study period.

Table 2.3: Characteristics of Emergency Department Presentation among Patients Age ≥65 Admitted from the Emergency Department for Treatment of Alcohol Withdrawal, Jan 2008-Mar 2012

	N = 145 cases
Means of arrival	
Walk-in	28 (19%)
Ambulance	106 (74%)
Other	5 (3%)
Not documented	6 (3%)
Accompanied to the ED	
Alone	90 (63%)
Family	16 (11%)
Home health aide / nurse	3 (2%)
Other	4 (3%)
Not Documented	32 (22%)
Chief Complaint in ED Triage	
Alcohol related	69 (48%)
Trauma related	43 (30%)
Psychiatric	19 (13%)
Other complaint	
Currently suicidal (n=124)	16 (13%)

Currently homicidal (n=124)	0 (0%)
Vital Sign Abnormalities in Triage	
Heart rate ≥100	57 (40%)
Blood pressure (SBP ≥160 or DBP ≥100)	46 (32%)
Both elevated heart rate and blood pressure during ED evaluation (HR ≥100 and (SBP ≥160 or DBP ≥100))	21 (14%)
Recognized as intoxicated at arrival (n=143)	
No	50 (35%)
Yes	44 (31%)
Not documented	49 (34%)

Results presented as n (%) unless otherwise specified.

Table 2.4: ED Assessment & Treatment among Patients Age ≥65 Admitted from the Emergency Department for Treatment of Alcohol Withdrawal, Jan 2008-Mar 2012

	N = 145 cases
Signs of Withdrawal Documented in ED attending examination	
Tremor (n=143)	
Documented and Present	46 (32%)
Documented and Not Present	14 (10%)
Not Documented	83 (58%)
Hyperreflexia (n=144)	
Documented and Present	1 (1%)
Documented and Not Present	1 (1%)
Not Documented	142 (99%)
Tongue fasciculations (n=144)	
Documented and Present	15 (10%)
Documented and Not Present	5 (3%)
Not Documented	124 (86%)
No documentation of assessment for withdrawal (tremor, hyperreflexia, or tongue fasciculations)	60 (41%)
Vital Sign Abnormality during ED evaluation	
Heart rate recorded ≥100	83 (58%)
Blood pressure recorded (SBP ≥160 or DBP ≥100)	62 (43%)
Both heart rate and blood pressure	42 (29%)

During ED evaluation (HR ≥100 and (SBP ≥160 or DBP ≥100))	
Blood Alcohol Level	
Ordered	87 (61%)
Level of positive results (mg/dL), median (IQR)	208 (103 – 265) Range: 5 – 449
Negative	33 (39%)
First Benzodiazepine ordered in ED	
Lorazepam	34 (23%)
Diazepam	40 (27%)
Chlordiazepoxide	18 (12%)
Benzodiazepine ordered in ED	
Lorazepam Only	17 (12%)
Diazepam Only	31 (21%)
Chlordiazepoxide Only	6 (4%)
Multiple	32 (22%)
None	59 (41%)

Table 2.4: (continued)

% of Patients with ED Diagnosis	
Alcohol Related	101 (70%)
Trauma	33 (23%)
Psychiatric	5 (3%)
Other	63 (43%)

Results presented as n (%) unless otherwise specified.

Table 2.5: Hospital Admission & Treatment among Patients Age ≥65 Admitted from the Emergency Department for Treatment of Alcohol Withdrawal, Jan 2008-Mar 2012

	N = 145 cases
Admitting Service	
Regular floor	95 (66%)
Step-down	27 (19%)
ICU	9 (6%)
Discharged directly from ED	4 (3%)
Other/not documented	10 (7%)
Benzodiazepine given during admission	
Lorazepam Only	38 (26%)
Diazepam Only	10 (7%)
Chlordiazepoxide Only	4 (3%)
Other	1 (1%)
Multiple	82 (57%)
None	10 (7%)
Alcohol withdrawal protocol followed	
CIWA* score calculated	58 (41%)
Consultations obtained during admission	
Trauma	1 (1%)
Psychiatry	34 (23%)
Social Work	75 (52%)
Length of Stay (days)	

Overall, median (IQR)	6 (4 – 10)
Discharged, median (IQR)	6 (4 – 11)
AMA, median (IQR)	2 (1 – 3)

Results presented as n (%) unless otherwise specified.

‘*’ Clinical Institute Withdrawal Assessment, possible range 0-67; withdrawal mild (≤15), moderate (16-20), severe (>20).

Table 2.6: Hospital Discharge & Readmission among Patients Age ≥65 Admitted from the Emergency Department for Treatment of Alcohol Withdrawal, Jan 2008-Mar 2012

	N = 145 cases
Discharge	
Home	80 (56%)
Nursing Home	11 (8%)
Acute Care Facility	4 (3%)
Subacute Care Facility	25 (17%)
Detox Facility/ Program	9 (6%)
AMA	9 (6%)
Death	2 (1%)
Other	3 (2%)
Not Documented	1 (1%)
Referrals in Discharge Note	
Alcoholics Anonymous	109 (76%)
Psychiatric Follow-up	23 (17%)
Primary Care Follow-up	108 (78%)
Specific Appointment in Note	44 (32%)
Re-presentation to the ED within 30 Days	
Any Reason	36 (25%)
Second presentation ED diagnosis	
Alcohol Related	18 (50%)

Trauma	10 (28%)
Psychiatric	3 (8%)
Other	14 (39%)

Results presented as n (%) unless otherwise specified.

DISCUSSION

The results of our study demonstrate that alcohol withdrawal is not restricted to younger adults, but also occurs in the elderly with sufficient severity that some patients require hospital admission and formal detoxification management. Further, a large proportion of patients re-present to the ED with both alcohol-related and other conditions within only 30 days. Our study also demonstrates that evaluations for AWS in the elderly are not uniformly done and protocols may be needed to systematically evaluate and treat these patients while in the ED. In addition to increasing awareness that AWS is a potential diagnosis in the elderly (and not prevalent only in younger adults), our study highlights the importance of timely interventions that should be priorities in the ED management of these patients.

Few other studies have considered AWS in the elderly. Our review of the literature over the last 3.5 decades found only 7 studies that addressed AWS in older adults.[9-15] However, these studies differed markedly in design, setting, and age inclusion criteria. As a result, little information could be extracted and complied in any systematic way; thus no conclusions about presentation and optimal management can be made. In order to begin to understand how to assess and treat older adults with AWS more effectively, a better characterization of this population is needed. Specifically, information is required to assist medical providers, particularly ED physicians, in identify these patients more readily upon presentation. In addition, analyzing their management in the ED and on the inpatient hospital service, as well as ascertaining their final disposition, is crucial towards the goal of optimizing their care.

Our study also showed that AWS occurs in a broad spectrum of older patients, including women, who traditionally are considered less likely to present to the ED for alcohol abuse.[29] It was also surprising to find that the majority of patients reported no illicit drug use. While this is based on self-report, it still warrants some thought, considering the high rates of concurrent drug and alcohol abuse in younger populations.[30] It is possible that elderly patients are more likely to abuse only alcohol. However, possible co-substance abuse should remain a concern and be investigated further in elderly AWS patients.

Several of our findings regarding comorbidity also are noteworthy. In particular, the prevalence of self-reported physical comorbidity was lower than expected. Perhaps this can be explained by insufficient primary care and continuity of care often found in patients with alcohol abuse, and thus lack of awareness and treatment for other diagnoses. This further highlights the need for clinicians to be more vigilant about possible occult diseases in elderly patients who do not report comorbidity. It also may be a marker for poor follow up secondary to alcohol abuse or some other substance abuse. These issues are important to consider particularly for conditions that are exacerbated by alcoholism, such as hypertension, coronary artery disease, liver disease, obesity, and diabetes.[31-33,34] With respect to mental health comorbidity, our findings are consistent with other reports documenting a high prevalence of concurrent psychiatric illness in patients admitted for AWS.[30] Also similar to other reports, we found that although 91% of our patients reported a history of alcohol use or abuse, only 15% had been previously admitted to a treatment facility. Non-participation in formal detoxification and

rehabilitation programs, irrespective of age, has been attributed to lack of access or lack of interest in stopping alcohol use.

Our study highlights additional considerations in the comprehensive evaluation of elderly AWS patients. One major issue is reliance on self-report and the lack of confirming information. In order to manage patients optimally, information about the events that prompted the ED visit is critical. However, in our study only 16% were accompanied to the ED by another adult. Relying on self-report assumes the patient is able to provide a full and concise history on his or her own. Ideally, additional sources of information should be sought whenever possible to ascertain what is cause and what is effect. For example, in our study, the chief complaint was trauma-related in 30% and psychiatric-related in 13%. Thus, it is of paramount importance that ED physicians screen elderly patients presenting with falls or other traumas, as well as those with psychiatric complaints, for alcohol abuse because it may be either the precipitating factor or a contributing factor for the etiology of their chief complaint.

Because a rigorous history may be lacking in elderly AWS patients, the role of the physical examination becomes critical. It was noteworthy that in our study few patients presented with both elevated blood pressures and tachycardia; unlike the typical dyad in younger adults with AWS. It is well known that, in general, older individuals are much less likely than younger individuals to mount an appropriate response to stressful situations because of either blunted age-related change in physiologic response and/or effects of baseline medications.[17,28] It is very likely that this can be extrapolated to AWS, in which case relying on traditional vital sign derangements, as markers

for AWS may not be appropriate in older patients. Additional research is needed to investigate this phenomenon further.

Our study also supports the need for a comprehensive physical examination and a standard ED protocol for evaluation and management of possible AWS in the elderly. This is so because ED physicians do not routinely consider alcohol use or withdrawal in older adults and subsequently may not do a physical examination targeted at withdrawal, such as assess for tongue fasciculations, which have been shown to be early indicators of alcohol withdrawal.[9,35] However, as noted above, which elements of the physical examination are most sensitive to AWS in the elderly have not been determined and should be investigated further. This certainly also is the case for the management of the elderly AWS patient. In our study, less than half of patients received benzodiazepines, the mainstay of treatment, while in the ED. On the other hand, almost a quarter received more than one benzodiazepine, which runs counter to well-studied guidelines for pharmacotherapy in older adults.[36] While providers may have been attempting to take advantage of the different onsets of action and half-lives, potential development of delirium is strongly increased by this approach. Future investigation into differences in outcomes in patients receiving one versus more than one benzodiazepine is necessary.

Our study also addressed the subsequent post-ED management of elderly AWS patients. The rate of admission to either an intensive care unit or a step-down unit was higher than what has been reported for younger adults.[37] This also was the case for the average length of stay.[9] This suggests that older adults are more likely to have a complicated in-patient course. However,

despite a more complex clinical scenario and the fact that alcohol dependence is classified as a DSM-V disorder and is associated with comorbid psychiatric conditions, most patients did not receive psychiatric consults during their admission. [30] Other studies have advocated that psychiatric consultation should be a mainstay for patients admitted with AWS.[38] This finding, along with the low referral rate to outpatient psychiatric follow-up, again reinforces a common theme in our study; namely, that clinicians do not approach older adults with alcohol abuse disorder and AWS the same way as they might with younger patients.

There are several limitations to our study. First, it was conducted in a tertiary care medical center and may not be generalizable to patients in other settings. Second, it was based on retrospective chart review and certain clinical aspects, such as physical examination, may have been done, but were not recorded. Third, we did not include patients admitted to the psychiatric service; these individuals most likely represent a subset of AWS that has different characteristics and management needs.

In summary, our study demonstrates that commonly held notions that elderly patients with AWS are more likely to have multiple comorbidities, live alone, and present with a traumatic or infectious complaints, is not universally correct. After describing an elderly population at our institution with a diagnosis of AWS, we see that, apart from living alone, the majority of patients did not have multiple comorbidities and most did not present with either trauma or infection. Perhaps ED physicians need to re-assess how they approach older adults, to raise their index of suspicion for alcohol withdrawal in this population, and to be more systematic and efficient in identifying older

adults with AWS. The overarching goals are to make the diagnosis of AWS as soon as possible and institute necessary therapy early in the patient's course while still in the ED.

References

1. Caputo F, Vignoli T, Leggio L, Addolorato G, Zoli G, Bernardi M. Alcohol use disorders in the elderly: a brief overview from epidemiology to treatment options. Experimental gerontology 2012;47:411-6.
2. Sarff M, Gold JA. Alcohol withdrawal syndromes in the intensive care unit. Critical care medicine 2010;38:S494-501.
3. Stehman CR, Mycyk MB. A rational approach to the treatment of alcohol withdrawal in the ED. The American journal of emergency medicine 2013;31:734-42.
4. Scott RB, Mitchell MC. Aging, alcohol, and the liver. Journal of the American Geriatrics Society 1988;36:255-65.
5. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Journal of clinical epidemiology 2009;62:e1-34.
6. Booth A, Clarke M, Dooley G, et al. The nuts and bolts of PROSPERO: an international prospective register of systematic reviews. Systematic reviews 2012;1:2.
7. van de Glind EM, van Munster BC, Spijker R, Scholten RJ, Hooft L. Search filters to identify geriatric medicine in Medline. Journal of the American Medical Informatics Association : JAMIA 2012;19:468-72.
8. King R, Hooper B, Wood W. Using bibliographic software to appraise and code data in educational systematic review research. Medical teacher 2011;33:719-23.

9. Foy A, Kay J, Taylor A. The course of alcohol withdrawal in a general hospital. QJM : monthly journal of the Association of Physicians 1997;90:253-61.

10. Wojnar M, Wasilewski D, Zmigrodzka I, Grobel I. Age-related differences in the course of alcohol withdrawal in hospitalized patients. Alcohol and alcoholism 2001;36:577-83.

11. Wetterling T, Driessen M, Kanitz RD, Junghanns K. The severity of alcohol withdrawal is not age dependent. Alcohol and alcoholism 2001;36:75-8.

12. Liskow BI, Rinck C, Campbell J, DeSouza C. Alcohol withdrawal in the elderly. Journal of studies on alcohol 1989;50:414-21.

13. Brower KJ, Mudd S, Blow FC, Young JP, Hill EM. Severity and treatment of alcohol withdrawal in elderly versus younger patients. Alcoholism, clinical and experimental research 1994;18:196-201.

14. Kraemer KL, Mayo-Smith MF, Calkins DR. Impact of age on the severity, course, and complications of alcohol withdrawal. Archives of internal medicine 1997;157:2234-41.

15. Ferguson JA, Suelzer CJ, Eckert GJ, Zhou XH, Dittus RS. Risk factors for delirium tremens development. Journal of general internal medicine 1996;11:410-4.

16. Kitani K. Hepatic drug metabolism in the elderly. Hepatology 1986;6:316-9.

17. Kinirons MT, O'Mahony MS. Drug metabolism and ageing. British journal of clinical pharmacology 2004;57:540-4.

18. Moore AR, O'Keeffe ST. Drug-induced cognitive impairment in the elderly. Drugs & aging 1999;15:15-28.

19. Pasero CL, McCaffery M. Managing postoperative pain in the elderly. The American journal of nursing 1996;96:38-45; quiz 6.

20. Alagiakrishnan K, Wiens CA. An approach to drug induced delirium in the elderly. Postgraduate medical journal 2004;80:388-93.

21. Inouye SK. Delirium in hospitalized older patients. Clinics in geriatric medicine 1998;14:745-64.

22. Jacobson SA. Delirium in the elderly. The Psychiatric clinics of North America 1997;20:91-110.

23. Leentjens AF, van der Mast RC. Delirium in elderly people: an update. Current opinion in psychiatry 2005;18:325-30.

24. Hamers JP, Huizing AR. Why do we use physical restraints in the elderly? Zeitschrift fur Gerontologie und Geriatrie 2005;38:19-25.

25. Frank C, Hodgetts G, Puxty J. Safety and efficacy of physical restraints for the elderly. Review of the evidence. Canadian family physician Medecin de famille canadien 1996;42:2402-9.

26. Maldonado JR, Sher Y, Ashouri JF, et al. The "Prediction of Alcohol Withdrawal Severity Scale" (PAWSS): systematic literature review and pilot study of a new scale for the prediction of complicated alcohol withdrawal syndrome. Alcohol 2014;48:375-90.

27. Becker HC. The alcohol withdrawal "kindling" phenomenon: clinical and experimental findings. Alcoholism, clinical and experimental research 1996;20:121A-4A.

28. Jarrett PG, Rockwood K, Carver D, Stolee P, Cosway S. Illness presentation in elderly patients. Archives of internal medicine 1995;155:1060-4.

29. Brady KT, Randall CL. Gender differences in substance use disorders. The Psychiatric clinics of North America 1999;22:241-52.

30. Regier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. Jama 1990;264:2511-8.

31. Stampfer MJ, Colditz GA, Willett WC, Speizer FE, Hennekens CH. A prospective study of moderate alcohol consumption and the risk of coronary disease and stroke in women. The New England journal of medicine 1988;319:267-73.

32. Urbano-Marquez A, Estruch R, Navarro-Lopez F, Grau JM, Mont L, Rubin E. The effects of alcoholism on skeletal and cardiac muscle. The New England journal of medicine 1989;320:409-15.

33. Mukamal KJ. Alcohol use and prognosis in patients with coronary heart disease. Preventive cardiology 2003;6:93-8.

34. Wei M, Gibbons LW, Mitchell TL, Kampert JB, Blair SN. Alcohol intake and incidence of type 2 diabetes in men. Diabetes care 2000;23:18-22.

35. Sullivan JT, Sykora K, Schneiderman J, Naranjo CA, Sellers EM. Assessment of alcohol withdrawal: the revised clinical institute withdrawal assessment for alcohol scale (CIWA-Ar). British journal of addiction 1989;84:1353-7.

36. Beers MH. Explicit criteria for determining potentially inappropriate medication use by the elderly. An update. Archives of internal medicine 1997;157:1531-6.

37. Monte R, Rabunal R, Casariego E, Lopez-Agreda H, Mateos A, Pertega S. Analysis of the factors determining survival of alcoholic withdrawal

syndrome patients in a general hospital. Alcohol and alcoholism 2010;45:151-8.

38. Webster R, Holroyd S. Prevalence of psychotic symptoms in delirium. Psychosomatics 2000;41:519-22.